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# Technical Pitfalls and Limitations of SPECT/CT

Lefteris Livieratos, PhD<sup>\*,†</sup>

The synergy of functional and anatomic information in hybrid systems has undoubtedly enhanced the diagnostic potential of radionuclide imaging in recent years, contributing to the advancement of SPECT/CT in clinical practice. Since the introduction of commercial SPECT/CT in the late 1990s, the field has seen rapid expansion and development toward multidetector CT subsystems, establishing the role of SPECT/CT as a routine imaging tool. It is, however, important to discuss possible challenges and technical limitations of such systems and how these influence imaging outcomes. In particular, the issues of patient motion and spatial misalignment of the SPECT and CT modalities, data corrections such as those for photon attenuation, and the choice of CT acquisition protocols in relation to radiation exposure are discussed in the article.

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## Introduction

Molecular imaging techniques with high sensitivity, such as SPECT and PET and structural imaging, such as CT and MRI, have long been used routinely as an aid to diagnosis and treatment assessment, and they are often used successively at various stages of the patient management pathway. Dual-modality imaging, also referred to as hybrid imaging, offers the combination of functional and structural information in a single scanning session, with multiple advantages for the diagnostic decision process.

The advantages of combining functional and anatomical images were recognized early on, leading to the development of software registration techniques based on fiducial markers or voxel similarity algorithms. These were initially used in neuroimaging to fuse functional PET and SPECT images with anatomical images from CT and MRI. The potential was also recognized in imaging of other organs; however, various complications related to the nonrigid movement of internal organs, the accuracy of patient positioning in two separate imaging sessions, and the variable performance of registration algorithms limited their application in areas outside the brain.

For several years, PET and SPECT have been increasingly combined with CT in hybrid imaging systems. Although

initially the combination of modalities was experimental, the rapid development of hybrid imaging systems of PET/CT and SPECT/CT has established both as diagnostic tools in routine clinical practice. Currently, the combination of PET and MRI in a single system is under clinical evaluation in sequential<sup>1</sup> and simultaneous<sup>2</sup> arrangement, whereas MR-compatible SPECT, because of its additional requirements for physical collimation, is still under development.<sup>3</sup>

Although the synergy of functional and anatomical information in hybrid systems has undoubtedly enhanced diagnostic potential, it is also important to discuss possible challenges and technical limitations of such systems. In particular, the issues of patient motion and spatial misalignment, data corrections such as for photon attenuation, and the choice of CT acquisition protocols in relation to radiation exposure are discussed in the following sections.

## Development of Hybrid SPECT/CT

As early as 1991, Hasegawa et al<sup>4</sup> introduced a prototype high-purity germanium detector system for combined anatomical (CT) and functional (SPECT) imaging. The system used a single detector for both modalities, thus enabling simultaneous emission-transmission data acquisition,<sup>5</sup> and it was possible to achieve object-specific attenuation correction (AC) of the SPECT data using dual-energy CT.<sup>6</sup> However, the use of a single detector material for data acquisition of both the modalities, despite being an innovative approach at the time,

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resulted in compromised performance for both SPECT and CT, a technological limitation that still exists in the design of a dual-modality single detector system. This was later addressed by a hybrid SPECT/CT system comprising separate state-of-the-art commercial components optimized for each modality.<sup>7</sup> The project led later to the introduction of the first commercial dual-modality system, in 1999, the GE Millennium VG Hawkeye<sup>8</sup> comprising a dual-head variable-geometry SPECT system mount on a slip-ring gantry together with an x-ray CT component operated at 140 kV and 2.5 mA. An innovation at the time, its limited CT slice thickness and slow rotation time resulting in relatively long CT data acquisition time was quickly surpassed by rapid developments in CT technology.

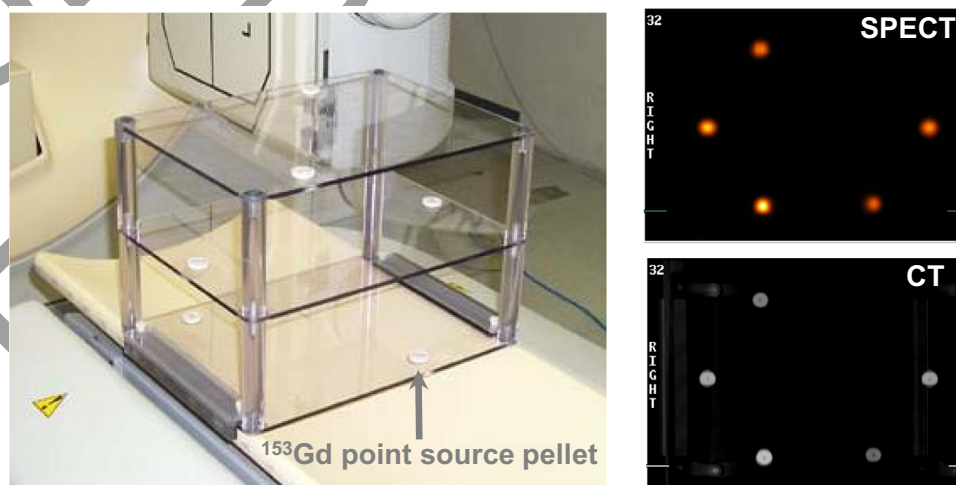
In parallel, efforts to integrate PET and CT had started approximately in 1998 with a prototype system<sup>9,10</sup> that made use of the slip-ring gantry of the ECART ART, a cost-effective design based on rotating partial ring of detectors. The system made use of a common rotating gantry to operate simultaneously the partial-ring PET and CT component with shared patient bed controlling axial translation to ensure minimal patient movement between the two scans. Despite hardware image coregistration being the primary aim of the system, the side issue of using CT for AC of PET had dramatic effects in shortening overall whole-body scan times, thus increasing patient throughput by a factor of three or more. The first commercially available PET/CT system was introduced in 2000 and coincided with approval of reimbursement in the United States for <sup>18</sup>F<sub>2</sub> scans in Oncology in 1999, thus elevating PET, until then a research tool confined mainly to neuroimaging, to its current level of an essential diagnostic tool in Oncology.

Although the first commercial SPECT/CT had introduced the concept of hybrid imaging in nuclear medicine, it was not until approximately 10 years ago when after speculation by individual groups,<sup>11,12</sup> SPECT/CT saw rapid expansion assisted by the introduction of commercial systems with high-end multislice CT imaging capabilities. For example, in the United

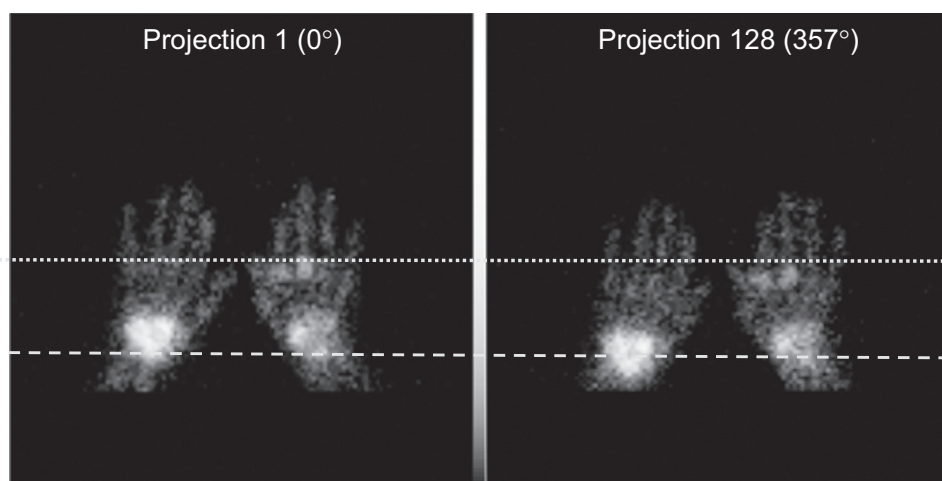
Kingdom, the trend over the past few years has been for replaced gamma camera to have multidetector CT components, a trend that seems to be supported by national audit data,<sup>13</sup> establishing SPECT/CT in routine clinical practice.

## Spatial Registration in SPECT/CT

Hybrid imaging systems rely entirely on the use of a common patient imaging bed, shared between two imaging systems that are otherwise independent, to ensure spatial registration of the two modalities and to achieve accurate image fusion. The two modalities are acquired sequentially with the patient remaining in the same position while the bed moves between the fields of view to be acquired. Therefore, establishing a spatial relationship between the two modalities is essential. This is usually performed during installation of the system and repeated periodically as part of a regular quality control program. Although the exact process may vary from one system to another, the basic principle relies on the use of markers detectable by both the modalities that are imaged at a fixed geometry (Fig. 1). These markers are often point sources containing a radionuclide detectable in SPECT as well as sufficient material density to result in detectable contrast in the CT images. After acquisition and reconstruction of the images, a computer algorithm is used to identify the center of each marker in both the modalities. The spatial transformation parameters that are necessary to make the marker centers overlap between the two modalities are calculated and saved onto the system. These transformation parameters (typically saved as rigid-body transformations, ie, three translations, three rotations, and three scaling or magnification factors) are then applied to all subsequent patient images, and assuming that there is no patient motion between modalities or other changes in system can achieve accurate spatial alignment and image fusion.



**Figure 1** Spatial registration phantom used in SPECT/CT to calculate intermodality transformation parameters. In this example, data from <sup>153</sup>Gd point sources that are also visible in CT are acquired for SPECT/CT spatial registration. The spatial transformation parameters that result in exact overlap of the marker centers in the two modalities can subsequently be applied to patient data for accurate registration and image fusion. (Color version of figure is available online.)



**Figure 2** SPECT projections at 0° and 357° from a typical  $^{99m}\text{Tc}$ -MDP SPECT study (corresponding to a time interval of 18 minutes), demonstrating the effect of gradual movement of the hands in the horizontal direction between the start and the end of the scan.

This method of *hardware registration* largely addresses limitations of data-driven *software registration* applied to images from separate scans, namely the nonrigid movement of internal organs and limited accuracy of reproducing patient positioning in two separate imaging sessions as well as the variable performance of data-driven registration algorithms and their dependency on image quality.

## Patient Motion in SPECT/CT

A crucial condition for accurate registration in SPECT/CT is that patient motion, whether gross movement or motion of internal organs, is minimal. In practice, however, both periodic and random patient motion cannot be fully eliminated.

Cardiovascular and respiratory motion (Figs. 6 and 8) as well as peristaltic motion and voluntary and involuntary muscular motion constitutes an inevitable problem, to a varying extent, for all imaging modalities. This is particularly true for the relatively long image acquisition times involved in SPECT,<sup>14</sup> typically in the range of several minutes, thus increasing the probability of organ motion during the scan (Fig. 2). In contrast, most modern systems can acquire multiple CT slices per rotation, often achieving acquisition of a reasonable axial view extend within a single-breath-hold (Fig. 6, Fig. 7). The effect of motion on the final image depends on the degree and nature of motion and can result in blurring of features especially visible in focal areas of uptake. An added complexity in sequential hybrid systems such as SPECT/CT is the effect of patient movement to the accuracy of spatial alignment between



**Figure 3** Fusion display of  $^{99m}\text{Tc}$ -MDP SPECT/CT images of the wrists demonstrating misalignment between the two modalities. (Color version of figure is available online.)





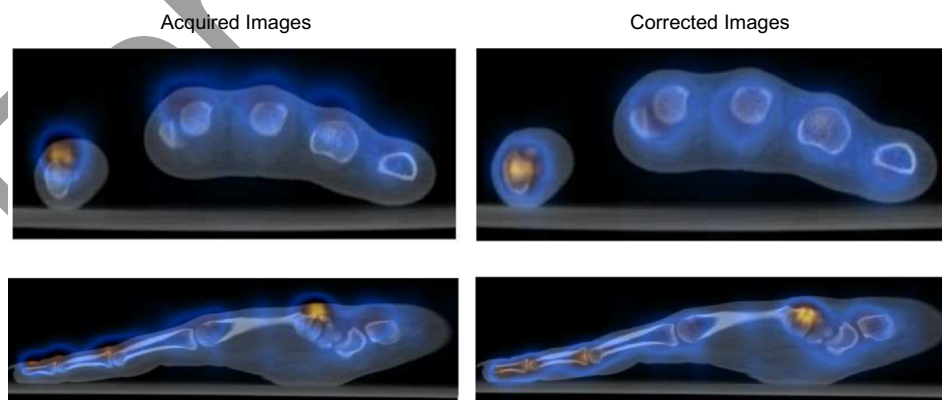
**Figure 4** Patient immobilization techniques should be used when necessary to restrict movement during scans and between modalities. These may include thermoplastic mesh (right) to restrict nonrigid movement. (Color version of figure is available online.)

the two nonsimultaneously acquired modalities.<sup>15–17</sup> For example, a sudden or gradual change from the starting scanning position affects the accuracy of spatial registration between the SPECT and the CT parts of the study. Often intermodality misalignment is more prone in body areas with many degrees of freedom for movement, such as the extremities (Fig. 3), where it is also more critical because of the fine nature of the anatomy in these areas.<sup>18</sup>

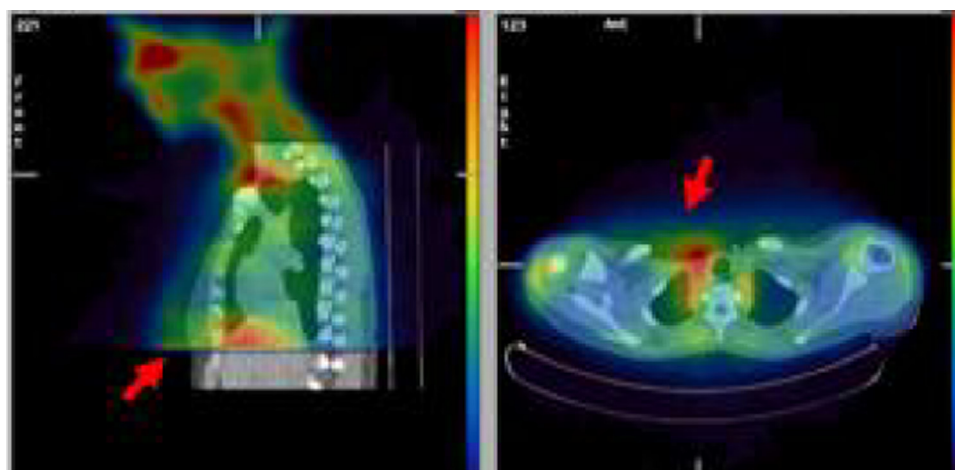
As patient motion cannot be completely eliminated, it is important to put appropriate measures in place to minimize its presence and its influence on the quality of diagnostic images. These measures may include the following:

- Patient positioning aids such as immobilization devices (Fig. 4).
- Data quality control including review of raw data and inspection of images for the presence of motion, often with the aid of physiological landmarks present in the data.
- Motion correction software may assist in restoring the quality of acquired data by monitoring fixed features in the data and applying corrections typically on the raw projection data as proposed in PET/CT<sup>19–21</sup> following respiratory gating.<sup>22–24</sup> Software registration techniques may be used to restore intermodality misalignment (Fig. 5); however, the accuracy of spatial registration achieved may be variable.

- Shortening of data acquisition protocols may reduce the prevalence of motion artifacts. Some aspects that may assist in this direction are, for example, the choice of collimator in SPECT and the image reconstruction regime. Recently, a number of studies have demonstrated significant advantages in image quality from reconstruction algorithms incorporating resolution recovery models, thus allowing shorter acquisition times of acceptable diagnostic quality.<sup>25–32</sup>
- Alongside the relatively long acquisition times of the emission part of a study, the technical specifications of the CT component or imaging protocol are also relevant to the way physiological motion influences patient data. Particularly in early SPECT/CT designs incorporating slow-rotating CT components mounted on the same gantry as the gamma camera, resulting CT acquisition times were in the range of several minutes. Although CT scan durations that are comparable to those of SPECT may compromise CT image quality, in other respects, acquiring the two modalities over similar breathing patterns (Fig. 8) may be an advantage, especially when CT images are used for AC of the SPECT, in which case, accurate spatial correlation of the two modalities becomes even more important. Potential developments in flat panel detectors<sup>33</sup> may help toward volumetric CT data acquisition matching that of SPECT.



**Figure 5** Fusion display of  $^{99m}\text{Tc}$ -MDP SPECT/CT images of the wrist (A) before and (B) after motion correction. (Color version of figure is available online.)



**Figure 6** Fusion display of CT and  $^{131}\text{I}$ -mIBG SPECT (free breathing) in sagittal and transverse views. (Color version of figure is available online.)

The effect of motion-related effects is closely related to the part of the anatomy and the particular application. For example, for bone imaging, respiratory motion, a well-documented cause of artifacts in imaging of the lung, liver, or heart is less likely to be a problem when imaging the skeleton. Causes of gross patient motion affecting the spatial alignment of SPECT to CT, such as long emission scans, patient discomfort, or inadequate patient immobilization, tend to be more important in bone imaging, though these can also affect cardiac imaging where CT data are used for AC of the SPECT images.

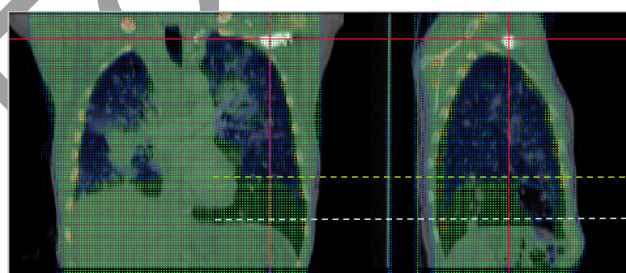
With the advent of PET/CT, the speculation of its use in image-guided radiotherapy has played a pivotal role, drawing awareness on the effects of patient motion. Despite application of SPECT/CT in image-guided radiotherapy in some cases (eg, Ref. 34), the topic has not received extensive speculation. Perhaps this fact, along with poorer spatial resolution of SPECT, may partly explain that the problem of patient motion afforded thus far limited or less coordinated technical attention. Given the volume of examinations, the extensive range of anatomy, and the multitude of clinical situations where SPECT/CT is now a clinical standard, the problem of motion should be considered a major technical challenge, and more technical resources should be put toward alleviating its effects.

## CT-Based Attenuation and Scatter Correction

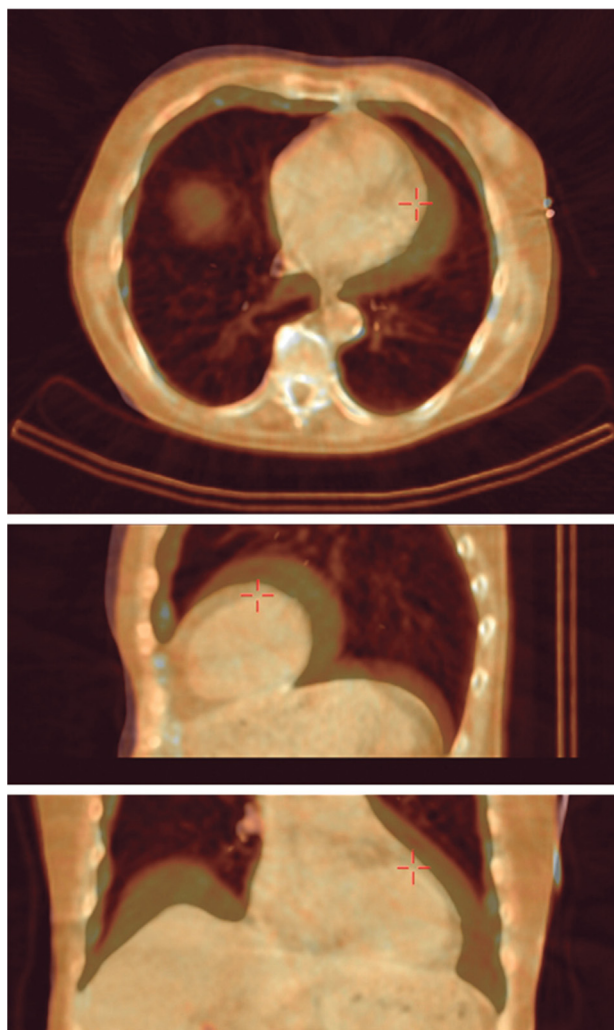
The macroscopic effects of photon attenuation and photon scatter in emission tomography originate at a microscopic level from photon interactions with the matter mainly through the Compton effect at energies relevant to SPECT.<sup>35</sup> The effect of photon attenuation, generally causing underestimation of the activity concentration that becomes more severe toward the center of the object, is well documented primarily in cardiac SPECT imaging.<sup>36–39</sup> The effect of photon scatter is an added background-like image component typically leading to an overestimation of activity concentration in low uptake areas, which may affect both contrast and quantification in SPECT studies.<sup>40</sup> Therefore, information from the CT can be used for correction of the attenuation and scatter of the emission photons. CT image contrast-forming Hounsfield Units (HU) are derived as

$$HU = 1000 \times \frac{\mu - \mu_{\text{water}}}{\mu_{\text{water}} - \mu_{\text{air}}}$$

where the linear attenuation coefficient  $\mu$  is measured for the relevant photon energies (mean energy for x-ray spectrum: 70–80 keV). Although CT measurements refer to photon



**Figure 7** Image fusion of CT data acquired with and without specific breathing instructions during scanning (separate imaging sessions two weeks apart) demonstrating respiration-related misalignment with potential effects onto SPECT localization and attenuation and scatter correction. (Color version of figure is available online.)



**Figure 8** Image fusion of CT data acquired over 60 seconds during tidal respiration (dark thermal image) and over 12 seconds during breath-hold at end expiration (grayscale). Images courtesy of Philips Medical Systems. (Color version of figure is available online.)

energies different to those of the emission data (eg, 140 keV for  $^{99m}\text{Tc}$ -labeled compounds) it is possible to scale into  $\mu$  values at the required energy for the radionuclide used. However, it is important to note that the energy dependency of  $\mu$  is different for each type of tissue (ie, soft tissue or bone); therefore, a differential scaling approach is required for each segment of  $\mu$  values. Typically, *bilinear scaling* is used to convert voxel values from HU to linear attenuation coefficients at the relevant emission photon energies with a scaling factor for soft tissue ( $\text{HU} \leq 0$ ) and another one for higher values ( $\text{HU} > 0$ ). When *bilinear scaling* is performed correctly, it results in an *attenuation map*, that is, an image of the distribution of  $\mu$  values for the energy of photons to be corrected for.<sup>41,42</sup> A reduction of the original CT spatial resolution to match that of SPECT is typically performed at this stage.

A CT-derived attenuation map may therefore be used for AC of SPECT data by incorporating the calculated levels of attenuation that a photon beam encounters through a specific path trajectory between the point of emission and the point of

detection. This step for CT-based AC can be incorporated in statistical reconstruction algorithms (iterative reconstruction) such as the maximum likelihood expectation maximization (MLEM)<sup>43</sup> or its accelerated version—the ordered subsets expectation maximization (OSEM)<sup>44</sup>—frequently used in the clinic. This is a difference from PET, where AC is feasible directly on projection data via a simple multiplication with the AC factor for the specific projection, thus allowing AC of PET images even with filtered back-projection techniques. Over the years, this difference has resulted in the false preconception of the inability of SPECT for quantification, stemming for the early times when iterative reconstruction, and hence AC, was not practically feasible.

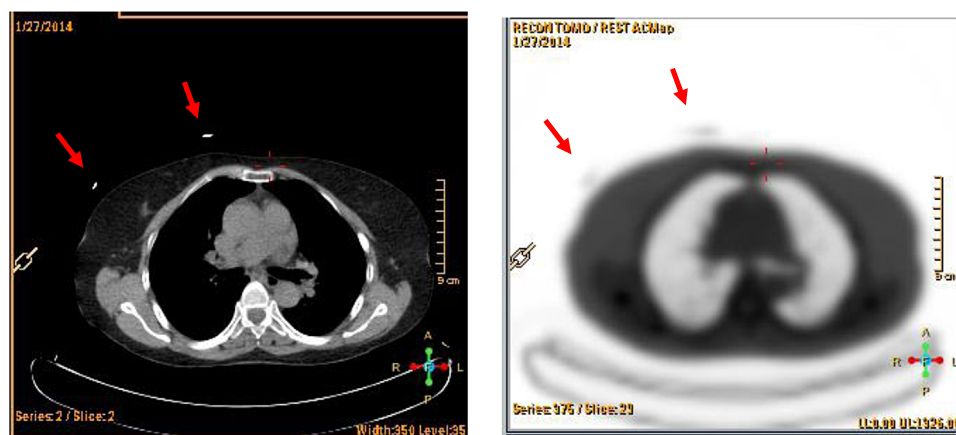
CT-derived attenuation maps may also be used to calculate the distribution of scatter photons, which can subsequently be subtracted from the raw emission data to achieve correction for photon scatter. It is important to note that the  $\mu$  values for narrow-beam geometry, which are typically stored as voxel values in an attenuation map, convey predominantly the attenuation of photons deflected outside the line of site to the detector but not those scattered into it. The latter (scatter component) is significant in realistic patient conditions corresponding to broad-beam geometry; hence, it is important that when possible, AC should be combined with scatter correction to achieve improved levels of accuracy.

As CT data in hybrid imaging can influence the accuracy of the emission data via attenuation and scatter correction, it is important to be aware of the image manipulation and processing steps involved and potential consequences extensively discussed in PET/CT.<sup>45–48</sup> For example, with the use of contrast agents or the presence of metallic or other prosthetic implants, the histogram of values of the CT images would be altered when compared with the normal histogram of CT numbers. This may subsequently affect aspects of CT data conversion to attenuation maps and therefore attenuation and scatter corrections.

An aspect of hybrid imaging, related to attenuation (and possibly scatter) correction, is partial truncation of the attenuation maps.<sup>49–51</sup> Although for anatomical localization only acquisitions of data over the areas of interest are required, for CT-based correction purposes, the acquisition of CT images with no truncation of the object is necessary. This is because the integral of the degree of photon attenuation along a certain projection is used to correct the projection data. Thus, for attenuation (and scatter) correction purposes, it is mandatory to use appropriate acquisition parameters to include the whole object in the CT field of view.

Highly attenuating materials such as metallic objects and prosthetics can be a source of inaccuracies by generating artifacts on the CT images. These may not only affect anatomical localization of the SPECT features but may also propagate further to affect the CT-derived attenuation maps and consequently introduce inaccuracies into the attenuation-corrected SPECT images. Although small metallic objects such as electrocardiogram leads seem to be dealt with by the conversion algorithms to be adequately represented into the attenuation map (Fig. 9), larger objects such



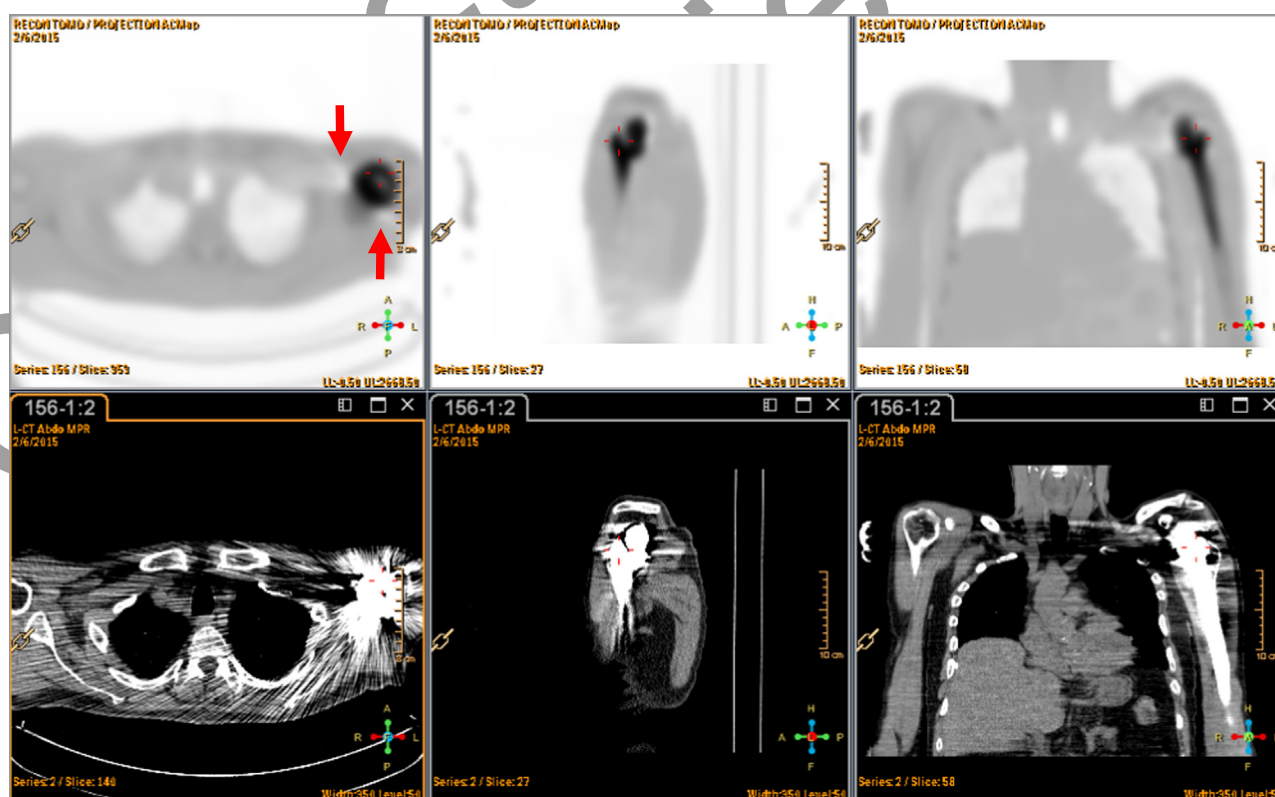


**Figure 9** Small metallic objects (ECG leads) in CT (left) and derived attenuation map (right). ECG, electrocardiogram. (Color version of figure is available online.)

as prostheses may introduce artifactual photopenic areas on the CT because of beam hardening, which can then appear as areas of low attenuation on the generated attenuation maps (Fig. 10). It is therefore essential to maintain awareness for such sources of artifacts and appropriate quality control of the data to highlight such cases. Technical advances such as iterative reconstruction of CT data or dual-energy CT<sup>52–54</sup> may bring further improvements in dealing with the repercussions from highly attenuating materials.

## CT Imaging Protocols and Radiation Exposure Considerations

Development of hybrid imaging was initially technology led rather than application driven, with early experimental attempts combining SPECT or PET with CT on the same system, not being profoundly insightful of a particular clinical diagnostic need. However, the need for faster transmission data



**Figure 10** Prosthetics artifacts (shoulder replacement) in CT and potential effects onto SPECT. Photopenic areas near high x-ray attenuation objects in CT (bottom row) are also retained in the attenuation maps (top row). Such artifacts may propagate onto SPECT images after CT-based attenuation correction. (Color version of figure is available online.)



**Table 1** Examples of CT Acquisition Protocols for a 16-Slice CT System Potentially for Use in Hybrid Imaging over a Range of Required Image Characteristics which May Influence Radiation Exposure

Protocol	Abdominal	Abdominal for Multiplanar Reconstruction (MPR)	Head and Neck
Voltage (kV)	120	120	120
mAs or slice	50	100	100
Tube rotation time (s)	0.5	0.75	0.5
Pitch	1.188	1.188	1.188
Slice thickness (mm)	3	1.5	2
Axial increment (mm)	3	0.75	1
Collimation	16 × 1.5	16 × 0.75	16 × 0.75
CTDI <sub>vol</sub> (mGy)	3.5	7.8	15.2
DLP (mGy·cm) per 10 cm axial scan	35	78	152
$E_{DLP}$ (mSv·mGy <sup>-1</sup> ·cm <sup>-1</sup> )	0.015 (abdomen)	0.015 (abdomen)	0.0023 (head) 0.0054 (neck)
Effective dose (mSv) per 10 cm axial scan	0.52	1.17	0.35 (head) 0.82 (neck)

CTDI<sub>vol</sub>, volume CT dose index.

acquisition for AC, particularly established in PET, and the enhancement of diagnostic outcome from the combined anatomical localization very soon formed the basis for clinical application of hybrid imaging. Furthermore, with the advancement of the capabilities of CT components to diagnostic quality levels similar to those of stand-alone CT systems, ideas for development of “one-stop-shop” imaging protocols also emerged. This means that currently the role of anatomical images in SPECT/CT and PET/CT spans a range of applications from AC, where limited image quality is necessary, to high-end image quality comparable to diagnostic stand-alone CT inevitably at the cost of increased radiation exposure to patients. Examples of three CT acquisition protocols each of which may form part of a SPECT/CT (or PET/CT) study are shown in Table 1. Differences in acquisition parameters may reflect diverse needs in image quality such as voxel resolution and signal-to-noise levels, which may vary for each clinical application. The influence of acquisition parameters in radiation exposure is reflected in the volume CT dose index and dose-length product (DLP)<sup>55</sup> indicated in the table per 10 cm of axial scan. DLP values have been converted to estimates of effective dose in mSv by using the effective dose conversion factors ( $E_{DLP}$ ) appropriate for each part of the body.

The right level to pitch the balance between radiation exposure and image quality depends on factors varied for each clinical application, which will hopefully become clearer as evidence is being published from clinical studies.

Nevertheless, a considerable increase in radiation exposure to the patient owing to the addition of CT<sup>56–59</sup> has been a major repercussion along the clinical benefits of SPECT/CT. A number of dose-saving schemes during CT acquisition have been developed over the years based on modulation of the x-ray tube exposure<sup>60,61</sup> based on the axial or angular (azimuthal) variation of the patient body thickness or overall attenuation derived typically from a scout planar image. Recent advances in statistical iterative reconstruction of CT data have shown a significant improvement in signal-to-noise levels to enable exploiting reduction of radiation exposure without loss of image quality.<sup>62–65</sup> However, owing to the different

treatment of the raw projection CT data by the iterative reconstruction algorithms and the novel levels of signal to noise that can be achieved, certain image quality characteristics such as pixilation and noise may appear different from the typical images reconstructed by analytical filtered back projection, which may require some assimilation and optimization of protocols as well as evaluation of reconstructed HU used as quantitative metrics in diagnostic radiology. For these reasons, hybrid imaging is ideally suited for early implementation of dose reduction by iterative CT reconstruction because of the existing culture for dose control typically away from high-end or high-exposure CT-only diagnostic protocols.

## Logistical Challenges Related to SPECT/CT Service Planning

Appropriate room design and radiation protection associated with the addition of CT in a nuclear medicine environment form a major logistical and cost consideration when introducing SPECT/CT service.<sup>66,67</sup> Other considerations at the planning stage involve addressing training requirements<sup>68–70</sup> that, depending on national or local regulations, may range from well defined and prescriptive to generic and vague. In some countries, operation of the CT component by the imaging technologists may require specified certification or predefined data acquisition protocols. Similarly, the use of intravenous CT contrast agents may require involvement of specified professionals. Despite the specific legal framework, staff training is considerably more complex and critical in SPECT/CT (eg, compared with conventional radionuclide imaging or PET/CT) because of the wide range of applications and clinical protocols available, which are often interleaved with preexisting imaging protocols such as planar spot views or whole-body scans.

Several years now into the transition from scintigraphy to dual-modality imaging, two distinct concepts for the use of SPECT/CT have been formed<sup>71</sup>: The use of CT at restrained radiation exposure to support anatomical localization of SPECT findings, often called *low-dose CT* or *localization CT*, is typically performed at low radiation exposure equivalent to

levels of CT effective dose of 1 mSv, thus constrained to rudimentary CT image quality for low signal-to-noise levels and compromised image slice thickness. At the other end, the use of diagnostic radiology-equivalent CT-guided by SPECT aims to fully optimize both modalities for diagnostic accuracy. In reality, implementation of local protocols may be anywhere in between these two concepts and the exact level at which this compromise is pitched may depend on the preferences of the local reporting and referring clinicians, the population mix and referring patterns, among others. Whatever the exact local protocols are, it is imperative that adequate training and expertise are available to clarify the exact requirements and to ensure that all means of radiation exposure reduction have been carefully applied. For example, it is superfluous to refer to an "attenuation correction" protocol delivering on average 5 mSv of radiation dose when perfectly adequate AC may be achieved with CT data of minimal radiation exposure. On the contrary, the variable localization requirements of different SPECT imaging applications have understandably led to a plethora of CT imaging protocols with a variety of radiation exposure profiles. As hybrid SPECT/CT finds its place in a range of disease clinical pathways alongside preexisting imaging methodologies, there will hopefully be sufficient clinical studies published to inform relevant guidelines and lead to an eventual stratification of imaging protocols and overall reduction of patient radiation dose. This may also help clarify referral criteria for SPECT/CT and reduce the conditional dependency from planar imaging (eg, proceeding to SPECT/CT based on the whole-body planar scan), thus further improving planning of resources and patient throughput.

## Discussion and Future Directions

Radionuclide imaging typically provide limited anatomical information, hampering precisely localization of otherwise highly specific functional findings. Hence, spatial registration of radionuclide images with high-resolution anatomical images in combined systems such as SPECT/CT has greatly enhanced the diagnostic imaging process<sup>72–76</sup> while overcoming limitations related to retrospective software registration such as patient positioning differences in separate scanners and the complexities of registration techniques departing from the typically nonrealistic rigid-body approach.

Despite that SPECT/CT was introduced commercially slightly ahead of PET/CT and a stronger case for hybrid imaging for SPECT (widespread use of clinical SPECT, poorer spatial resolution, and often highly specific tracers with limited anatomical information from physiological uptake), early scanner designs had initially a limited clinical impact. Perhaps the fact that SPECT was already clinically established and widely available was an impediment in that the paradigm shift was being too wide and expectations for quantitative imaging and research applications rather subdued. Early SPECT/CT designs were therefore limited initially to rudimentary low-cost CT component with limited capability for diagnostic-quality CT imaging. However, the past decade has seen a shift and

redefinition of SPECT/CT with the introduction of diagnostic-quality multidetector CT subsystems.

However, the advantage of the hardware approach in combined systems of the two modalities being inherently registered would always benefit from an inquisitive approach to ensure that these basic assumptions remain valid on a case-by-case basis.<sup>15–18</sup> Patient motion, whether unexpected or physiological such as respiration, may add inaccuracies and require constant monitoring and quality control to eliminate its effects. Although accurate motion correction schemes based on monitoring devices or data-driven approaches become more generally available in future, these will have to prove their merit in the clinical setting and contribute improvements to image quality in a simple, efficient, and ideally unsupervised manner. Although PET/CT has seen a considerable interest in developing such approaches,<sup>77–80</sup> the extra complexity of SPECT/CT and in particular the sequential rather than simultaneous sampling of projection data over the subject has so far rather limited interest toward this direction.<sup>81–83</sup>

The availability of spatially coregistered CT data has opened new directions for SPECT with more accurate and quantitative imaging regimes.<sup>84–89</sup> Although AC has been implemented in SPECT for many years now with radionuclide external transmission sources and iterative reconstruction, the use of CT-based attenuation and scatter correction offers improved accuracy and reliability away from problems associated with decaying external transmission sources. Such corrections, together with improved signal-to-noise levels and spatial resolution recovery demonstrated in recent years by the use of more sophisticated image reconstruction algorithms,<sup>25–32</sup> have greatly enhanced what can be achieved in SPECT imaging. What remains now is a change of mindset so that SPECT/CT quantification features in the type of questions that we expect to answer in nuclear medicine.

Admittedly, along with significant benefits, the combination of SPECT and CT has brought important repercussions such as a notable increase in overall radiation dose to the patient from the combined study and entangled workload planning logistics along with increased technical and reporting complexity. However, recent advances in statistical iterative reconstruction of CT data can bring up significant reduction to radiation exposure without loss of image quality along with existing dose-saving schemes. In fact, hybrid imaging is ideally suited for early implementation of dose reduction by iterative CT reconstruction owing to the existing culture for dose control typically away from high-end or high-exposure CT-only diagnostic protocols. As hybrid SPECT/CT imaging matures and its clinical utility becomes more widespread and established, detailed understanding of its technical challenges further improves and this can only lead to development of solutions to overcome limitations for more accurate diagnostic imaging.<sup>33</sup>

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